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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,293	01/09/2001	Thomas E. Wagner	035879-0116	5976

22428 7590 06/15/2004

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/756,293	WAGNER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *The proposed amendment would raise new issue under 35 U.S.C. § 112, second paragraph*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *32,35,36,41 and 44*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

JANICE LI
PATENT EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because: The arguments to rejections under 35 U.S.C. § 112, 1st and 2nd paragraphs are moot because the proposed amendments have not entered.
With respect to rejection under 35 U.S.C. § 103, applicants argue that the method described by Koolwijk et al comprises using a Percoll density gradient centrifugation, which is more time consuming than the single step HAT selection as described by Gong et al, that Koolwijk discussed mutant phenotype that does not apply to the hybrid cells of Gong et al, that the PDG centrifugation is critical in the Koolwijk method because it increases the production of hybrid hybridomas about 8 fold.
The arguments have been carefully considered but found not persuasive because Koolwijk et al not only teach the disadvantage of mutant phenotype selection, but also teach the disadvantage of a biochemical selection which encompasses the HAT selection taught in Gong reference. Koolwijk et al teach that addition of biochemical inhibitors may not conduce the outgrowth of hybrid cells, and their disclosed method obviates the need for using biochemical inhibitors. The PDG centrifugation is a routine procedure in a cell biology laboratory, only takes 20' to perform, thus, in view of the potential harzard of using biochemical inhibitiors on the hybrid cell formation, it would not have been a burden for the ordinary skilled to use FACS alone or in combination with PDG centrifugation. Further, the 8-fold increase was compared to the process of cell sorting with or without the centrifugation, thus, the centrifugation is an enhancement for the hybrid cell production, but is not critical for cell fusion and selection. The ordinary skilled would be motivated to avoid the involvement of the biochemical inhibitor in view of the teaching of Koolwijk et al by substituting HAT with FACS.
Applicants go on to argue that at the time of filing, the fused cells were usually selected by metabolic selection, not the FACS, thus, one would not look to substitute a common prior art method with one more experimental approach for cell fusion selection. In response, the Koolwijk reference was published in 1988, by the time of the instant effective filing date, FACS selection for double stained fusion cells has become a well-known means in cell biology, thus, is not considered an experimental approach. Applicants then argue that Gong et al fail to recognize the significance of preserving antigen diversity in dendritic fusions and culturing cells over a period of time results in loss of tumor antigen diversity. In response, the claims as written encompass prolonged culture in the fusion step (step C), thus, applicants are arguing limitations that are not in the claims. Further, it is noted that in the specification, the tumor cells were cultured for an unknown period of time before fusion, thus the antigen diversity could have been lost even before the fusion. Moreover, in the claims, the starting neoplastic cell population is not limited to fresh isolated cells, thus, the antigen diversity may have been at least partially lost even before the fusion. Accordingly, for reasons of record and set forth above, the rejection stands.